AMENDMENTS TO THE CLAIMS:

The following listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1-49. (Canceled)

50. (New) A method for obtaining an optimized immunomodulatory polynucleotide, comprising:

(a) creating a library of mutant polynucleotides from at least two nucleic acids, wherein each nucleic acid encodes a B7-1 (CD80) protein and the nucleic acids differ from each other in at least two nucleotides;

(b) introducing the library of mutant polynucleotides into a genetic vaccine vector that encodes an antigen to form a library of vectors;

(c) introducing the library of vectors into cells;

(d) expressing the library of vectors on the cells;

(e) screening the library to identify at least one optimized mutant polynucleotide encoding a mutant B7-1 protein that is a costimulator having an improved ability to activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity through CD28 and a decreased activity through CTLA-4 compared to a B7-1 protein encoded by a nucleic acid from which the library was created;

(f) recombining at least one optimized mutant polynucleotide from (e) with at least one further mutant polynucleotide from (a) to produce a further library of mutant polynucleotides;

(g) screening the further library of mutant polynucleotides of (f) to identify at least one further optimized mutant polynucleotide encoding a mutant B7-1 protein that is a costimulator having an improved ability to activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity through CD28 and a decreased activity through CTLA-4 compared to a B7-1 protein encoded by a nucleic acid from which the further library was created; and

(h) repeating (f) and (g), if necessary, to identify at least one further optimized mutant polynucleotide encoding a mutant B7-1 protein that is a costimulator having an improved ability to

activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity through CD28 and a decreased activity through CTLA-4 compared to a B7-1 protein encoded by a nucleic acid from which the further library was created.

51. (New) A method for obtaining an optimized immunomodulatory polynucleotide, comprising:

(a) creating a library of mutant polynucleotides from at least two nucleic acids, wherein each nucleic acid encodes a B7-2 (CD86) protein and the nucleic acids differ from each other in at least two nucleotides;

(b) introducing the library of mutant polynucleotides into a genetic vaccine vector that encodes an antigen to form a library of vectors;

(c) introducing the library of vectors into cells;

(d) expressing the library of vectors on the cells;

(e) screening the library to identify at least one optimized mutant polynucleotide encoding a mutant B7-2 protein that is a costimulator having an improved ability to activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity through CD28 and a decreased activity through CTLA-4 compared to a B7-2 protein encoded by a nucleic acid from which the library was created;

(f) recombining at least one optimized mutant polynucleotide from (e) with at least one further mutant polynucleotide from (a) to produce a further library of mutant polynucleotides;

(g) screening the further library of mutant polynucleotides of (f) to identify at least one further optimized mutant polynucleotide encoding a mutant B7-2 protein that is a costimulator having an improved ability to activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity through CD28 and a decreased activity through CTLA-4 compared to a B7-2 protein encoded by a nucleic acid from which the further library was created; and

(h) repeating (f) and (g), if necessary, to identify at least one further optimized mutant polynucleotide encoding a mutant B7-2 protein that is a costimulator having an improved ability to activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity

through CD28 and a decreased activity through CTLA-4 compared to a B7-2 protein encoded by a nucleic acid from which the further library was created.

52. (New) A method for obtaining an optimized immunomodulatory polynucleotide, comprising:

(a) creating a library of mutant polynucleotides from at least two nucleic acids, wherein each nucleic acid encodes a B7-1 (CD80) protein and the nucleic acids differ from each other in at least two nucleotides;

(b) introducing the library of mutant polynucleotides into cells in conjunction with a genetic vaccine vector that encodes an antigen;

(c) expressing the antigen and the library of mutant polynucleotides on the cells;

(d) screening the library of mutant polynucleotides to identify at least one optimized mutant polynucleotide encoding a mutant B7-1 protein that is a costimulator having an improved ability to activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity through CD28 and a decreased activity through CTLA-4 compared to a B7-1 protein encoded by a nucleic acid from which the library was created;

(e) recombining at least one optimized mutant polynucleotide from (d) with at least one further mutant polynucleotide from (a) to produce a further library of mutant polynucleotides;

(f) screening the further library of mutant polynucleotides of (e) to identify at least one further optimized mutant polynucleotide encoding a mutant B7-1 protein that is a costimulator having an improved ability to activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity through CD28 and a decreased activity through CTLA-4 compared to a B7-1 protein encoded by a nucleic acid from which the further library was created; and

(g) repeating (e) and (f), if necessary, to identify at least one further optimized mutant polynucleotide encoding a mutant B7-1 protein that is a costimulator having an improved ability to activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity through CD28 and a decreased activity through CTLA-4 compared to a B7-1 protein encoded by a nucleic acid from which the further library was created.

53. (New) A method for obtaining an optimized immunomodulatory polynucleotide, comprising:

(a) creating a library of mutant polynucleotides from at least two nucleic acids, wherein each nucleic acid encodes a B7-2 (CD80) protein and the nucleic acids differ from each other in at least two nucleotides;

(b) introducing the library of mutant polynucleotides into cells in conjunction with a genetic vaccine vector that encodes an antigen;

(c) expressing the antigen and the library of mutant polynucleotides on the cells;

(d) screening the library of mutant polynucleotides to identify at least one optimized mutant polynucleotide encoding a mutant B7-2 protein that is a costimulator having an improved ability to activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity through CD28 and a decreased activity through CTLA-4 compared to a B7-2 protein encoded by a nucleic acid from which the library was created;

(e) recombining at least one optimized mutant polynucleotide from (d) with at least one further mutant polynucleotide from (a) to produce a further library of mutant polynucleotides;

(f) screening the further library of mutant polynucleotides of (e) to identify at least one further optimized mutant polynucleotide encoding a mutant B7-2 protein that is a costimulator having an improved ability to activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity through CD28 and a decreased activity through CTLA-4 compared to a B7-2 protein encoded by a nucleic acid from which the further library was created; and

(g) repeating (e) and (f), if necessary, to identify at least one further optimized mutant polynucleotide encoding a mutant B7-2 protein that is a costimulator having an improved ability to activate a T cell response induced by the genetic vaccine vector and exhibiting an increased activity through CD28 and a decreased activity through CTLA-4 compared to a B7-2 protein encoded by a nucleic acid from which the further library was created.